

## Scientific Abstract

### **A Phase I/II Dose-Escalation Trial of Intratumoral Injection with a Replication-Deficient Adenovirus Vector, Ad-mda7 (INGN 241) In Combination with Radiation Therapy In Patients with Locally Recurrent Breast Cancer**

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This open-label, Phase I/II, dose-escalation study is designed to evaluate the safety and determine the maximum-tolerated dose (MTD), cellular transduction, and expression of transgenic protein of the adenovirus vector encoding MDA-7, Ad-mda7 (also known as INGN 241), when the vector is administered via intratumoral injection (ITI) in combination with radiation therapy to patients with locally recurrent breast cancer. The antitumor activity of INGN 241 will be evaluated based on evidence of intratumoral viral transduction of tumor cells as detected by polymerase chain reaction (PCR) and reverse transcriptase polymerase chain reaction (RT-PCR) assays, and expression of the melanoma differentiation associated protein (MDA-7) as detected by immunohistochemistry. The effect of this combination therapy on tumor growth, pharmacokinetics of INGN 241 DNA, MDA-7 protein, and the humoral immune response to INGN 241 will be evaluated in order to better understand their effects on both safety and efficacy.

Patients with primary inoperable breast cancer refractory to neoadjuvant chemotherapy or recurrent carcinoma of the breast with gross disease will be eligible for enrollment. All patients will receive from 50 - 60 Gy of radiation. In the Phase I portion of the study, three patients will be enrolled in each of three cohorts at doses of INGN 241 of  $2 \times 10^{10}$  virus particles (vp),  $2 \times 10^{11}$  vp, and  $2 \times 10^{12}$  vp. INGN 241 will be locally administered into the tumor region being treated during the course of radiation at day 0, day 21, and day 42. One injection site will be used for every 1 cm of tumor, permitting a range of 1 - 6 total injections sites per lesion. Tumors exceeding 6 cm will be injected at only 6 sites. For the Phase II portion, X patients will be enrolled at the MTD with the primary outcome measure being clinical and pathological response rate.

Patients will be requested to undergo fine needle aspirates and core biopsies of the tumor tissue to be treated prior to the Adv-mda-7 / radiation treatment. Additional post-treatment tissue from the treated tumor site will be obtained with fine needle aspirates and core biopsies on day 3 and during the gene therapy administrations at day 21 and 42.

This gene transfer construct has been previously used in human subjects, in the ongoing open label Phase I study the INGN 241 has been well tolerated to date.